EP-131 - DIVERSITY AND NS5B NATURAL POLYMORPHISMS IN HCV VIRUSES DRIVING THE CURRENT EPIDEMIC IN PORTUGAL

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Background: HCV genotype identification and characterization of NS5B resistance-associated substitutions (RASs) occurring as natural polymorphisms are crucial for establishing the treatment outcome and duration and which patients may benefit from treatment with direct acting antivirals (DAAs), sofosbuvir and dasabuvir.

Methods: Direct sequencing of HCV NS5B gene was performed on plasma samples collected retrospectively from a cross-section of 230 DAAs-naïve patients attending a central hospital in Lisbon, Portugal. HCV sequences were subtyped and analysed for sofosbuvir and dasabuvir RASs and polymorphisms. Phylogenetic analysis including transmission cluster identification (maximum likelihood) and time-scaled phylogeny (Bayesian estimation) were also performed to delineate the current HCV epidemic.

Results: Majority of the patients (94.8%; n=218) harbored viruses with baseline NS5B polymorphisms. For dasabuvir, C316N was the single RAS and was observed in 31.4% (n=11) GT1b-infected patients. Amino acid substitutions on scored position for sofosbuvir V321I, V321I/V and V321S/L were identified in one patient each; these patients were infected with GT1a clade I, GT1a clade II and GT3a, respectively. Time to the most recent common ancestor (MRCA) suggests that subtypes 1a, 3a and 4a prevailed in the Portuguese HCV epidemic after the 1950's probably in association with the intravenous drug use (heroine) epidemic in Portugal.

Conclusions: This study highlights possible influence of HCV subtypes to DAAs resistance which could be relevant to improved therapeutic interventions based on DAAs combined therapy.